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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,408	03/12/2001	Mathew F. Ogle	1416.20US01	1108

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EXAMINER
NAFF, DAVID M

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,408	OGLE ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 & 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/20/03 has been entered.

The amendment filed 11/20/03 amended claims 1, 10, 16, 34 and 36.

Claims examined on the merits are 1-28 and 34-43 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28 and 34-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Adequate support is not found in the specification for reciting "bridges are generally non-reactive with other bridges" in claims 1, 16, 34 and 36. Applicants refer to page 6, lines 7-13, as providing support. However, this section of the specification discloses that functional groups of the bridges are generally non-reactive with other bridges, and not that bridges are non-reactive with other bridges.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 and 34-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "the bridges are generally non-reactive with other bridges", is uncertain as to meaning and scope. It is uncertain as to an amount of non-reactivity required and reactivity excluded by the term "generally". This term is vague, and its metes and bounds are relative and subjective. Additionally, it is uncertain as to bridges that are other bridges the bridges are generally non-reactive with. The claims appear to be requiring a plurality of bridges to be non-reactive with another plurality of bridges.

Claim 1 is confusing by not having clear antecedent basis for "the bridges" in line 3. Line 2 recites "a bridge molecule" which requires only one bridge molecule.

Claim 10 is unclear how it further limits claim 1 by requiring the linkers to be active with respect to the tissue since in claim 1 the linkers are bonded to the tissue. How can inkers be active to tissue after being bonded to the tissue? If the linkers are active before bonding to the tissue, this is inherent, or otherwise the linkers would not bond to the tissue.

Claim Rejections - 35 USC § 103

Claims 1-28 and 34-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogle et al (5,958,669) in view of Yang et al (5,935,168) for reasons in the previous office actions of 5/20 and 10/27/03 and for reasons herein.

The claims are drawn to tissue containing linkers bonded to tissue and bridge molecules bonded between two or more of the linkers, to a method of crosslinking tissue to prepare the tissue having linkers and bridge molecules, to tissue containing modified sites having bridge molecules bonded to two or more of the modified sites, and to a method of crosslinking tissue to prepare the tissue having modified sites and bridge molecules. In all these embodiments, the bridges are required to be generally non-reactive with other bridges.

Ogle et al disclose crosslinking tissue to fix tissue by reacting the tissue with glutaraldehyde.

Yang et al disclose crosslinking tissue with glutaraldehyde, and then reacting with a diamine followed by reacting with additional glutaraldehyde (col 1, line 43 and claims 8-10).

After reacting with glutaraldehyde as disclosed by Ogle et al, it would have been obvious to react with a diamine and then with additional glutaraldehyde as suggested by Yang et al. This will result in the diamine being a linker and the glutaraldehyde being bridge. Additionally, after initially crosslinking with glutaraldehyde some free aldehyde groups will remain that will react with the diamine and result in the glutaraldehyde being a linker and the diamine being a bridge. The aldehyde groups of a glutaraldehyde with not react with other aldehyde groups of another glutaraldehyde, and the amine groups of a diamine will not react with amine groups of another diamine. This will result in a bridge not reacting with another bridge.

Response to Arguments

Applicant's arguments filed 11/20/03 have been fully considered but they are not persuasive.

Applicants urge that Ogle et al and Yang et al do not teach glutaraldehyde as a linker and bridge molecules that are different from the linker. However, the invention as broadly claimed in claim 1 and other dependent claims does not require glutaraldehyde as a linker. In these claims, the linker can be a diamine and the glutaraldehyde a bridge as clearly results when reacting with a diamine and glutaraldehyde in Yang et al. As to dependent claims that

may require glutaraldehyde as a linker, some aldehyde groups would remain free after crosslinking in Ogle et al and the diamine would react with these free aldehyde groups to result in glutaraldehyde being a linker and the diamine being a bridge. This is supported by the specification disclosing (page 24, lines 21-22) that the linker and bridge molecule can be applied to the tissue sequentially. If both ends of glutaraldehyde react with tissue as asserted by applicants, then this embodiment will not work since the tissue is contacted with the glutaraldehyde in the absence of the bridge molecule as in Ogle et al and Yang et al. The fact that this sequential embodiment works supports that some free aldehyde groups will remain after crosslinking tissue with glutaraldehyde as disclosed by Olgle et al and Yang et al.

Applicants urge that free aldehyde groups will not remain after crosslinking as disclosed by Ogle et al since Ogle et al selected glutaraldehyde oligomers of a size to span the gap between sites to fix the tissue. However, the glutaraldehyde oligomers of Ogle et al can contain oligomers of 3 monomers (col 6, line 37) which will be less than 25 Angstroms as disclosed in the present specification. To obtain a length of less than 25 Angstroms and preferably between 2 and 10 Angstroms as disclosed in the specification (page 13, lines 5-7) would require screening as disclosed by Ogle et al. The claims do not require a different length linker than the glutaraldehyde of Olgle et al and Yang et al. Additionally, the glutaraldehyde oligomer of Ogle et al will contain glutaraldehyde monomer in combination with the

oligomer, and the monomer will also be within the Angstrom range disclosed in the specification. As is apparent from instant claim 24, treatment with the linker can be as long as one month. This is clearly a longer time than the 6 days used by Ogle et al (col 9, line 6). When treating with a glutaraldehyde linker, the present claims encompass fixing tissue in the same way as Ogle et al. As to Yang et al rinsing, the raising will not remove glutaraldehyde having one aldehyde group bound to tissue, and the other aldehyde group not bound to tissue and being free.

Applicants urge that claims 34-37 require bridge molecules bonded to two or more modified sites of the tissue. However, this encompasses the embodiment shown by Fig 2 of Yang et al where glutaraldehyde bridges free amine groups of diamines reacted with activated carboxyl groups of tissue. The claims do not specify how modification is accomplished, and modified sites could be formed by reacting carboxyl groups of tissue with a diamine as disclosed by Yang et al. As to claims 35 and 37 that require modified sites to comprise aldehyde groups, this would encompass first crosslinking tissue with glutaraldehyde and then reacting with a diamine as in Yang et al. As noted, free aldehyde groups will remain after crosslinking, and the claims do not exclude activating carboxyl groups before adding the diamine. Ogle et al and Yang et al nowhere disclose that some free aldehyde groups do not remain after crosslinking. If applicants obtain free aldehyde groups after reacting glutaraldehyde with tissue

for one month, it would clearly be expected that free aldehyde groups will remain after reacting for 6 days as in Ogle et al

In regard to a diamine being a linker and glutaraldehyde being a bridge molecule, applicants urge that glutaraldehyde is a known linker as taught in Ogle et al and Yang et al. However, neither of these references use the term "linker" when referring to glutaraldehyde. While crosslinking may inherently involve linking, reacting with a diamine as disclosed by Yang et al also inherently involves linking. Since the diamine links the tissue to glutaraldehyde, the diamine can also be considered a crosslinker. There is no recognition in the prior art that a linker function requires a crosslinking agent such as glutaraldehyde and that a bridging function requires a diamine. A linker is inherently a bridge molecule and a bridge molecule is inherently a linker.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
2/14/04